

ART. XXIV.—*Recent Works on Albuminuria and the Testing of Urine.*

1. *On the Various Modes of Testing for Albumen and Sugar in the Urine.* Two lectures by GEORGE JOHNSON, M.D. London, 1884.
2. *On Bedside Urine Testing, including Quantitative Albumen and Sugar.* By GEORGE OLIVER, M.D., 2d ed. London, 1884.
3. *Discussion on Albuminuria, its Pathology and Clinical Significance, before the Glasgow Pathological and Clinical Society.* Reprinted from the *Glasgow Medical Journal*. Glasgow, 1884.

It may be said without exaggeration, that whatever is worth knowing about albuminuria is contained in the three small volumes above named. It is true that the reader who has perused them all may be in some uncertainty in view of the large number of facts which are there brought to his notice, as to exactly what ought to be remembered. Only a few years ago it would have been thought scarcely possible that so much new information could have been gathered upon this important subject, in connection with the tests for it, the mechanism of its production, and its bearing upon health and disease. Unfortunately, as is so often the case, when a mass of new facts are adduced upon a given subject, there are some discrepancies in the results of different observers, which time and further experience must reconcile.

Dr. Johnson's admirable little book is practically an appeal for picric acid for the first place, not only as an albumen test, but also as a delicate test for sugar, although other methods of testing for albumen and sugar are also considered. He demonstrates the usual fallacies and defects of the heat and nitric acid tests, and calls attention to a source of error which is not commonly appreciated. It is the practice of adding acetic acid to the urine before boiling, as the result of which an acetate of albumen is formed, which, like the nitrate of albumen, is not coagulable by heat. The albumen, therefore, remains in solution, and is not detected. This statement of Dr. Johnson is confirmed by our own experience.

Dr. Johnson very properly insists that the smallest amount of albumen detectable, whether accompanied or not by the presence of tube-casts, is abnormal. For its detection, into a test-tube six inches long, he pours a four-inch column of urine; then holding the tube in a slanting position, he gently pours an inch of the saturated picric acid solution on the surface of the former, where, in consequence of its low specific gravity (1005), it mixes only with the upper layer of the urine. As far as the yellow color of the picric acid solution extends, the coagulated albumen renders the liquid turbid, contrasting with the transparent unstained urine below. There must be an actual mixture, and not merely a surface contact of the two liquids. When, in consequence of the scantiness, the turbidity is slight, the application of heat to the upper part of the turbid column increases the turbidity. If the tube be then placed aside, in the course of an hour a delicate horizontal film will have formed at the junction of the colored and unstained strata of urine.

Another method recommended by Dr. Johnson, is to add about one-third of a grain of powdered picric acid, or as much as can be carried on the point of a penknife, to about a drachm of urine in a test-tube. As the picric acid dissolves, the urine becomes turbid in proportion to the amount of albumen.

The albuminous opalescence, which always *occurs immediately* if at all, and is increased by heat, may easily be distinguished from the coarse granular particles of urate of sodium, which sometimes result from the acidity of the picric solution, since they are readily dissipated by heat. If left alone they also fall quickly to the bottom, carrying with them so much of the picric coloring matter, that when placed under the microscope they are so opaque as to appear almost black.

In like manner, peptones, quinine, and the other vegetable alkaloids, which are precipitated by picric acid, are redissolved on the application of heat. In fact, says Dr. Johnson, "there is no known substance occurring in either normal or abnormal urine, except albumen, which gives a precipitate with picric acid insoluble by the subsequent application of heat." Further, out of some hundreds of specimens of urine he has tested for peptones, he has found them in only one specimen, which was sent to him by Dr. Oliver.

Dr. Johnson believes, too, that picric acid is a much more delicate test for peptones than Fehling's copper solution, which has been chiefly relied on.¹

While peptones and urates are redissolved by applying heat, both are redeposited on cooling, when the urates are revealed by the microscope to be composed of large granules of sodium urate and uric acid crystals, while the peptones appear as exceedingly minute granules, which exhibit the Brownian movement. If peptones are associated with albumen in the same specimen, their detection and separation may be readily effected by the picric acid and heat tests. The precipitate with picric acid, instead of being increased and rendered dense by heat, as when albumen alone is present, will be lessened in proportion to the peptones present. If the boiling liquid be then poured on a filter, the dissolved picrate of peptones will pass through and precipitate again on cooling, while the coagulated albumen remains on the filter.

Dr. Johnson considers the addition of citric acid to the picric solution, as suggested by Dr. Oliver, unnecessary. This may be so, but it is nevertheless true, as Dr. Oliver says, that the picric cum citric solution is more delicate than the picric alone. That is, in testing very small albuminurias, we have found the picric acid solution to which citric acid has been added in the proportion of two drachms to the ounce of the former to produce a broader and more distinct line when used by the contact method than does the pure picric acid solution. At the same time, while the urine experimented with was one which, although it contained numerous hyaline tube-casts, did not respond to the heat and pure acid tests, the line produced by the picric solution was as distinct as any one could desire. Another advantage, also, of the mixed picric and citric solution is the fact that it is heavier than any urines likely to be met with; and, therefore, may be placed first in the test-tube and overlaid with urine; while the pure picric acid solution, which has a specific gravity of 1005, is lighter than most urines, and must, therefore, be poured on the urine. Again, a urine may be so light as to be of the same specific gravity as the picric solution, when it is impossible to overlay at all, the two fluids mixing immediately. This is by no means unimportant, because it seems to be conceded by all observers that the "contact method" is that which in-

¹ If urine is gently poured on the surface of some Fehling's solution previously introduced into a test-tube, a *rose-red color* appears at the junction of the two liquids if peptones are present.

sures the greatest delicacy with all the so-called delicate tests, and without which most of them can scarcely be called delicate.

Dr. Oliver's little book, which reached a second edition within a twelve month after it first occurred to him to facilitate urinary examination at the bedside by means of test-papers, is ostensibly devoted to this subject, but contains much valuable information quite independent of it, including quantitative methods for albumen and sugar, also by means of test-papers.

In Dr. Oliver's experience with the delicate tests he found the potassio-mercuric iodide, sodium tungstate, the picric cum citric and the picric acids the readiest; and he would, if asked for a preference, decide in favor of the first. He found the nitric acid, acidulated brine of Dr. Roberts, and potassium ferrocyanide, much slower in bringing to light mere traces of albumen. In the form of a test-paper, Dr. Oliver found the picric acid "the weakest of the series." In reply to this, Dr. Johnson says the small slips of paper dried after immersion in a saturated solution, do not retain sufficient to render them a satisfactory means of testing. But the ferro-cyanide of potassium, although much less delicate than the others mentioned, is the only one of the series besides heat and nitric acid which does not throw down peptones. For previous acidulation of the urine, Dr. Oliver invariably uses citric acid, which in the case of the potassio-mercuric iodide and potassium ferrocyanide is placed in a separate test-paper, which may be attached by a thin layer of rubber to the paper containing the reagent. This may be done in the case of the picric acid and sodium tungstate, although with them chemical reasons do not necessitate the separation of the citric acid from the reagent, and the two are, therefore, united in the same paper.

It is to be remembered that all of these tests may produce an opacity by the precipitation of acid amorphous urates, that all except the sodium tungstate and ferrocyanide of potassium precipitate the vegetable alkalis, and all but the ferrocyanide throw down peptones; but the opacity thus produced is promptly dissipated by moderate heat. The oleo-resins, as balsam of copaiba, are precipitated by citric and picric acids, but disappear on boiling to quickly reappear, even before the urine is quite cooled. The others of the series do not precipitate the oleo-resins, in the absence of citric acid.

Mucus is promptly precipitated by citric acid, and if this is added first, as directed by Dr. Oliver, the pressure of mucus is revealed at the onset, and it may be filtered out. The mucus thus precipitated is insoluble by heat, and is thus distinguished from urates. Heat, on the other hand, intensifies, the albumen precipitates. Dr. Kirk in his paper before the Glasgow Medical Society also suggests the use of citric acid to remove mucus.

With regard to quantitative testing for albumen, while, as far as we know, Dr. Oliver's method is the shortest and simplest yet suggested, we think it still too troublesome to be much availed of by the practising physician, and quite agree with Dr. Johnson, that for practical purposes it is sufficient to use the term "opalescence" for the slightest degree of coagulation, "miliness" for a greater degree of turbidity, and to indicate still larger amounts by fractions showing the proportion of the bulk of albumen, after subsidence, to the whole column of fluid tested, as $\frac{1}{2}$, $\frac{1}{4}$, etc. The latter mode of measurement may be carried to a considerable degree of

refinement by using suitably graduated test-tubes. Under these circumstances, at least six hours should be allowed for subsidence.

The discussion on Albuminuria before the Glasgow Pathological and Clinical Society is a 12mo. volume of 164 pages, made up of excellent papers, not, of course, unconflicting, or without error, but reflecting, every one, a high degree of intelligence, and a thorough acquaintance with urinary pathology. It is of course impossible for us to give even an outline of the views expressed by the different speakers, who included Dr. Roberts, of Manchester, Profs. Gardner, Greenfield, McCall Anderson, Hamilton, Cleland, Leishman, and Drs. David Newman, J. Mortimer Granville, Mahomed, Finlayson, Coats, McGregor-Robertson, Kirk, Perry, Middleton, and Steven; while papers by Drs. George Oliver and Francis Henderson were held as read in their absence, and published. It is but right to say, that some of the strongest papers were read by men whose names are least known.

We were somewhat surprised to find Drs. Newman and Middleton adopting the view originally suggested by von Wittich,¹ according to which the urine is formed in the first place by a filtration into the Malpighian capsule of the serum of the blood, including the albumen, and that the act is completed by the reabsorption of the albumen by the cells of the convoluted portions of the uriniferous tubules. This view we first met fully developed in the *Manual of Physiology*, by Küss, of which a translation by Dr. Amory, of Boston, was published in this country in 1875. The strongest argument in favor of it is the very satisfactory manner in which it explains the existence of the so-called normal or physiological albuminuria, but as we agree with Dr. Johnson and others, that no albuminuria can be physiological, although there may be an albuminuria which is of comparatively small significance, this prop of the von Wittich's theory is removed.

The most important point in Dr. Roberts's paper is the conclusion to which he has come, that the heat test remains in his hands the most delicate. But it appears to us, as to Dr. McCall Anderson, the president, that Dr. Kirk has thoroughly vindicated the delicacy of the picric acid test when used in the "contact method" as suggested by Dr. Johnson, and we can say also with Dr. Anderson, that "we know no more beautiful or more delicate test for albumen than the picric acid solution."

Both Dr. Johnson's and Dr. Oliver's books include sugar testing. The former gives the preference over all other tests to picric acid, for quantitative and qualitative testing. Being more delicate than Moore's test, the fermentation test, and Trommer's test, it is at least as delicate as Fehling's cupric fluid and Pavy's ammonio-cupric method, while it requires less manipulative skill, is more rapidly completed, and is not affected by albumen, uric acid, or other ingredient of the urine.

We must refer the reader to Dr. Johnson's own book for the details of the quantitative method by picric acid, but subjoin the method by which he tests every specimen of urine qualitatively, first for albumen, and then for sugar. To about a drachm of urine, add its own volume of saturated picric acid solution. If the liquid remains clear, no albumen is present. If a precipitate occurs, not dissolved by boiling, there is albumen in proportion to the amount of precipitate. Now add half a drachm of liquor potassæ, and boil for a few seconds; the coagulated albumen if present, is

¹ Ueber Harnsecretion und Albuminurie, Virchow's Archiv, Bd. x., s. 325, 1856.

dissolved by the alkali, and a red-black coloration occurs. If, when an ordinary half inch test-tube is held up to the light, a red color is visible through the liquid, there is no more than the normal amount of saccharine matter—less than a grain to the ounce. As little as two grains to the ounce will render the liquid inky-black, so that no light is transmitted through the tube.

Dr. Johnson believes, with many others, that there is a trace of glucose or some allied substance in normal urine, which gives a reaction alike with picric acid and Fehling's solution. He finds the results with the two tests remarkably uniform, that with picric acid indicating a little less, .5 to .7 of a grain to the ounce, and Fehling's solution, .7 to .9 of a grain. We think there is reason to believe that such reaction with Fehling in normal urine is due to uric acid, and possibly in part to kreatinin; and that when these substances are carefully removed, no reaction occurs with Fehling. Dr. Johnson is sustained in his position that uric acid does not react with picric acid, by the results of Dr. Oliver's experiments; but the latter has found that both kreatin and kreatinin reduce the alkaline picric solution by the aid of heat. As the daily secretion of kreatinin in the urine is 11.5 grains, according to Thudicum, and 9 to 20 grains according to Neubauer, it is not at all unlikely that the reaction found by Dr. Johnson between normal urine and picric acid may be due to this substance.

Dr. Oliver's test for sugar is the intensely blue, indigo carmine, or the sulph-indigotate of sodium, in the shape of a test-paper, since the test is not available in the aqueous form.

The effect of glucose upon the indigo-carmine is, in the presence of heat, to decolorize it, producing in the course of such decolorization a characteristic play of colors, which may even be availed of for the quantitative estimation of sugar. One, or at most two drops of diabetic urine introduced into a solution made by covering one of the test-papers with water, and gently heating it, will cause, within a minute after the first simmer, a beautiful violet tint to spread throughout the bright-blue solution; very quickly, the violet deepens and passes into purple; this, in its turn, melts into reddish-purple, which gives place to various tints of red, orange, and finally a straw-color, which remains without further change however long the fluid is heated. Now, on shaking the tube, the colors return in the inverse order to that in which they appeared, a result which is due to the reoxidation of the indigo.

The reaction is truly a beautiful one, but for further details we must refer the reader to Dr. Oliver's little book, adding here that the test-papers, both for albumen and sugar testing, may now be obtained in this country, of Parke, Davis & Co., neatly packed in a box along with a graduated test-tube and dropping-tube, and directions for their use.

Dr. Oliver has carefully compared this test with Fehling's, which he regards as the best glucose test, with results indicating equal delicacy. Further, he has compared the behavior of the indigo-carmine, the cupric and picric tests, when boiled in the presence of various substances. These are his results:—

Of the constituents of normal urine found as giving *no reaction with indigo-carmine or Fehling*, are urea, kreatin, kreatinin, urates, chlorides, phosphates, unoxidized sulphur, hippuric acid, sulphates, lactates, oxalates, ammonia, butyric acid. Of these, kreatin and kreatinin reduced the alkaline picric solution. *Indigo-carmine remained unchanged, but Fehling*

was reduced by uric acid, oxalic acid, and lactic acid. Of constituents of abnormal urines, leucine, tyrosin, albumen, peptones, non-saccharine bile, blood, pus, and mucus gave no reaction with indigo-carmin or Fehling. Indigo-carmin, Fehling, and picric acid were all reduced by ammonium sulphide. Indigo-carmin and picric acid were reduced by inosite, and Fehling was turned olive-green by it. Of other substances, cane-sugar, pure glycerine, mannate, boiled starch, gum acacia, glycyrrhizin, and salicin produce no reaction with indigo carmine or Fehling, while gum acacia reduces picric acid, and milk-sugar and dextrin reduce all three. Of medicinal substances quinine, morphia, codeia, atropin, caffeine, santolin, strychnine, balsam of copaiba, benzoate of lithia, hypophosphates, iodides, liquor pepticus, ether, and arbutin, exhibit no reaction with indigo-carmin and Fehling. Iron sulphate, gallic and tannic acids reduce all three reagents. Indigo is unaffected while Fehling is reduced by chloroform, resin, carbolic acid, sodium salicylate, jalapin, and chloral. *The urine of persons taking chloral hydrate reduces Fehling's solution*, the bismuth test, and salts of silver. In summary, out of 64 substances experimented with, Fehling was reduced by 15, picric acid by 11, and indigo-carmin by 8.

The quantitative testing by the indigo papers is only claimed by Dr. Oliver to be approximate. To us it seems troublesome, but so much depends in these matters upon habit and personal experience, that it is not fair to judge from such a limited opportunity as our own. To the practitioner, any test requiring apparatus even slightly specialized, is apt to be discarded for that which requires only simple tubes. We hold that for sugar some kind of quantitative testing is absolutely necessary, and the simpler the means by which it can be accomplished, the more likely are those means to be used. With Fehling's solution a sufficiently accurate quantitative estimation of sugar may be made with the test-tube and graduated measure, or even graduated test-tube and the spirit lamp. Even Dr. Johnson's standard fluid and apparatus, simple as they are, are in the way of the availability of the picric acid for quantitative testing. Other things being equal, the test of the value of a test is its availability. Each of the three tests is sufficiently accurate if intelligently handled, while perhaps the Fehling's solution requires most skill in its use for small quantities of sugar, and we await with interest the result of a year's experience of the profession with them, after they have become sufficiently known.

J. T.

ART. XXV.—*The Diagnosis of Diseases of the Spinal Cord.* By W. R. GOWERS, M.D., F.R.C.P., Assistant Professor of Clinical Medicine in University College, Physician to University College Hospital, and to the National Hospital for Paralyzed and Epileptics. Third edition, pp. 92. Philadelphia: P. Blakiston, Son & Co., 1884.

THE admirable manual of Dr. Gowers, issued in 1879, has done much to stimulate the intelligent study of diseases of the cord, and that such a guide was really wanted is shown by the exhaustion of two large editions within four years. The only important change in this edition is a new section on the diagnosis of functional from organic lesions of the cord, to which